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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,268	09/29/2003	Michael Fantuzzi	33503/US	3101

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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
01/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/674,268	FANTUZZI, MICHAEL	
	Examiner	Art Unit	
	ROSANNE KOSSON	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,15,18-20,22,23,32-34,36-43 and 45-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,15,18-20,22,23,32-34,36-43 and 45-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/23/09; 5/18/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS of 12/17/10*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 17, 2010 has been entered. Claims 14, 18, 22, 33, 34, 36, 45 and 46 have been amended. Claims 1-13, 16, 17, 21, 24-31, 35 and 44 were canceled in previous Office actions. Claims 52-55 have been added. Accordingly, claims 14, 15, 18-20, 22, 23, 32-34, 36-43 and 45-55 are examined on the merits herewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 42, 45, 52 and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the aforementioned claims, except for claim 45, recite a composition that is a soft gel comprising about a 30% solution of coenzyme Q10 (co Q10) in

limonene. Claim 45 recites a composition that is a soft gel comprising about a 25% solution of co Q10 in limonene. These limitations are not present in the application as filed, with or without about before the percentage, and are therefore new matter. Paragraphs 17 and 18 of the as-filed specification (which are the paragraphs cited by Applicant as providing support for the amended claims) provide support for the other ranges and concentrations recited in the amended claim set, as these paragraphs disclose the other concentrations that are the upper and lower limits of the ranges recited in the instant claim set. The concentrations in the specification may be combined to create new ranges. But, the aforementioned claims recite data points that are new, that are not present in these paragraphs, and that, as a result, may not be combined with other data points to create new ranges. THIS IS A NEW MATTER REJECTION. New matter is prohibited, and Applicants are required to cancel new matter from the claims (see MPEP 608.04).

Claim Rejections - 35 USC § 103

In view of Applicant's amendments to the claims, the rejections in the previous Office action are replaced with the rejections below. These rejections are similar to the previous rejections and have been modified to mirror the amended claims.

Claims 14, 15, 18, 20, 22, 23, 32-34, 36, 42, 43, 45 and 46 remain rejected, and claims 52-55 are rejected, under 35 U.S.C. 103(a) as being unpatentable over Soft Gel Technologies, Inc. (EP 888774) in view of Garti et al. (US 2003/0232095 A1), Elstner (WO 02/09685 A1 or English language equivalent US 2004/0047922 A1) and RITO Partnership (Rice Bran Oil Info, http://web.archive.org/web/20020809203831/http://www.ricebranoil.info/why/index.html, web page of Aug. 9, 2002, printed from the Internet on April 29, 2009). This rejection has been discussed in the previous Office actions.

To reiterate, Soft Gel discloses a soft gel (soft gelatin capsule) comprising co Q10 dissolved in rice bran oil and Vitamin E, another oil that is a tocopherol and an anti-oxidant. Thus, Soft Gel teaches a solution of co Q10 in two carriers that are oils. The three components are mixed before encapsulation so that soft gel capsules containing 30 mg of co Q10 and 30 IU of vitamin E are produced (see p. 2, lines 5-7 and 51-52; and p. 3, lines 4-5). When co Q10 is dissolved in a plant oil, the bioavailability is improved over a dry formulation, as shown by increased blood levels of co Q10 in subjects receiving the soft gel capsules (see p. 2, lines 31-45; p. 3, lines 4-6; p. 3, line 54, to p. 4, line 16; and Tables I and II). Soft Gel does not disclose dissolving the co Q in d-limonene.

Garti et al. disclose compositions, nano-scale emulsions, comprising co Q10 dissolved in d-limonene (see paragraphs 10-16, 29 and 40-42 and claim 9; d-limonene, (R)-limonene and (+)-limonene are synonyms). These compositions are nutritional supplements whose absorption by the body and bioavailability are better than those of solid dosage forms (see paragraphs 3-7). The advantage of these formulations is that they are stable and can be diluted in either oil or water while maintaining their structure (see paragraphs 10-16, 29, 30 and 40-42). The working examples of Garti et al. (see pp. 5-7) suggest that d-limonene is the preferred solvent among the large number of aromatic fruit and vegetable oils listed as solvents for lipophilic neutraceuticals in the aforementioned paragraphs. Thus, the idea of dissolving co Q10 in limonene (d-limonene) is not novel to Applicant, as is it is disclosed by Garti et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to replace the rice bran oil of Soft Gel with the d-limonene of Garti et al., because Garti et al. disclose that d-limonene is solvent for co Q10 that may be used in a nutraceutical formulation to deliver more co Q10 to the body. Garti et al. teach the functional equivalence of the two solvents. It is obvious to dissolve a compound in a solvent in which it is known to be soluble.

Moreover, RITO Partnership discloses that the main components of rice bran oil are palmitic, linoleic and linolenic acids (see Table 1). Garti et al. disclose that additional solvents for co Q10 are fatty acids of 2-24 carbons (see, e.g., paragraphs 16 and 29). Thus, Garti et al. teach the equivalence of d-limonene and long chain fatty acids as solvents for co Q10.

Further, Elstner discloses a nutraceutical composition comprising co Q10 dissolved in a mixture of γ-terpinene (an isomer of d-limonene derived from lemon oil, limonene being derived from orange oil) and vitamin E (alpha-tocopherol). Elstner discloses that vitamin E improves the anti-oxidant effect of the co Q10 and that his composition has an unexpected synergistic effect as an antioxidant in the circulatory system (see p. 3, line 24, to p. 5, line 15 of the PCT application or paragraphs 11-18 of the US application). As Elstner teaches dissolving co Q10 in a mixture of γ-terpinene (an isomer of d-limonene) and vitamin E, the artisan of ordinary skill would have expected co Q10 to be soluble in a mixture of d-limonene and vitamin E. See claims 14, 15, 18, 20, 22, 23, 32-34, 36, 42, 43, 45, 46 and 52-55.

Regarding the concentration ranges recited in claims 14, 18, 22, 32-34, 36, 42, 43, 45, 46 and 52-55 (the broadest of which is 15-60% by weight of co Q10 in the limonene solution, the narrowest of which is 30-45%, and the lowest of which is 15-40%), Garti et al. do not disclose the solubility limit of co Q10 in d-limonene. They disclose, however, that, in the concentrated form of their composition, the oil phase contains 2.45% co Q10 and 17.22% d-limonene, as percentages of the whole (see paragraph 40). But, the ranges recited in the claims do not appear to be associated with any particular result or effect. It would have been obvious to one of ordinary skill in the art at the time of the invention to dissolve as much co Q10 as possible in the d-limonene and in the solvent mixture of limonene and vitamin E, in order to make the most concentrated preparation possible, in order to deliver as much co Q10 as possible to the body. The solubility limit of co Q10 in any solvent or solvent mixture would have

been readily determined by the artisan of ordinary skill, such a determination being routine in the art. The maximum solubility of a compound in a solvent or solvent mixture is an inherent property of that liquid. Additionally, it would have been obvious to the artisan of ordinary skill at the time of the invention to dissolve as much co Q10 as needed to make a therapeutically effective solution or gel fill, even if this concentration is not the maximum one. The determination of a therapeutically effective concentration is also routine in the art for one of ordinary skill.

Regarding claim 22 and its dependent claims (23, 42, 43 and 45, 46, 54 and 55), which recite a neutraceutical composition packaged with instructions, because the composition of Soft Gel is a neutraceutical, it would have been obvious to the artisan of ordinary skill at the time of the invention to package it for sale as neutraceutical, along with instructions for its use.

In his arguments, Applicant argues independent claims 14 and 22 only and notes that the patentability of the dependent claims rests in the independent claims. Applicant asserts that the claimed invention is not obvious, because Garti et al. disclose that, in their emulsion, the amount of co Q10 is 2.45%, which is less than the ranges recited in the claims. In reply, as discussed in the previous Office actions, Garti et al. disclose that the ratio of co Q10 to d-limonene by weight is 2.45:17.22, which is a ratio of about 14:100. That is, this ratio maintains a stable oil phase in the emulsion. Because the oil phase is dispersed throughout the emulsion, the oil phase is not the same as a 14% solution. But, as discussed in the previous Office actions, determining the solubility of co Q10 in limonene would have been routine for the artisan of ordinary skill. It would have been obvious to the artisan of ordinary skill to make a solution that is as concentrated as possible, in order to provide a nutraceutical that is as potent as possible. Applicant has not demonstrated any unexpected or surprising results with his

nutraceutical composition compared to prior art compositions. Consequently, the claimed ranges are obvious limitations.

Applicant asserts that the claimed invention is not obvious, because Garti et al. disclose that, in their emulsion, the amount of co Q10 is 2.45%, and multiple components are required to achieve even this concentration. Applicant asserts that the prior art teaches that the solubility of co Q10 in any oil is many-fold lower than 2.45%. In reply, regarding the latter, Applicant has not cited any support for this comment. Applicant has not presented a reference or set of references disclosing the solubility of co Q10 in different oils. Regarding the former, as discussed in the previous Office actions and responses, the emulsions of Garti et al., similarly to any emulsion, comprise a hydrophilic solvent, a hydrophobic solvent and at least one emulsifier. As also previously discussed, Garti et al. had the purpose of making a stable co Q10 emulsion that was stable as a concentrate and that could be diluted by any amount in an oil or in water. The purpose was not to make an emulsion having the maximum amount of co Q10. Therefore, Garti et al. do not teach that the components of their emulsion are necessary for yielding a maximum co Q10 concentration of 2.45%.

Applicant has repeated his argument that Garti et al. teach away from the invention, because they teach an emulsion comprising 2.45% co Q10. In reply, this point was addressed in the previous Office actions and is addressed above. To reiterate, Garti et al. were cited for their teaching of d-limonene as a preferred solvent for co Q10. The claimed soft gel is the soft gel of Soft Gel Technologies, Inc., in which the rice bran oil is replace by limonene. But, that limonene is a solvent for co Q10 is taught by Garti et al. and is not novel to Applicant. Because of the teaching of Garti et al., substituting limonene for rice bran oil is an obvious substitution and is not inventive at the level of skill of one of ordinary skill in the art. Applicant further asserts that Garti et al. teach that the concentration of co Q10 in their emulsion is far better than what

one would have expected with limonene or any other oil. But, Applicant provides no support for this statement or the location of this sentence in the reference.

Applicant's comments on p. 10, first paragraph, of the Response are confusing. Applicant refers to the emulsion of Garti et al. as having both the minimal solubility and the maximum concentration for co Q10 in d-limonene. Applicant's point is not clear, and, therefore, this argument is not persuasive of patentability.

In view of the foregoing, a holding of obviousness is again required.

Claims 19, 37-39, 41, 47-49 and 51 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Soft Gel Technologies, Inc. (EP 888774) in view of Garti et al. (US 2003/0232095 A1) and Elstner (WO 02/09685 A1 or English language equivalent US 2004/0047922 A1).

To reiterate, the teachings of Soft Gel, Garti et al. and Elstner are discussed above. The idea of dissolving co Q10 in limonene (d-limonene) is not novel to Applicant, as is it is disclosed by Garti et al. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to add d-limonene to the composition of Soft Gel, to make a three-part solvent of d-limonene, vitamin E and rice bran oil for the co Q10, rather than the two-part solvent disclosed by Soft Gel (rice bran oil and vitamin E, rice bran oil being the carrier), because Garti et al. disclose that d-limonene is a solvent for the co Q10 and a preferred solvent compared to other fruit and vegetable oils. Thus, the artisan of ordinary skill would have had every expectation of success in dissolving co Q10 is this three-solvent mixture. It would have been obvious to one of ordinary skill in the art at the time of the invention to supplement the soft gel fill of Soft Gel by adding d-limonene, because Garti et al. disclose that co Q10 is soluble in d-limonene, and it is obvious to dissolve a compound in a solvent in which it is known to be

soluble. Garti et al. disclose of number of solvents for co Q10, while Soft Gel discloses the solvents rice bran oil, vitamin E and soybean oil. Optimization of solvent mixtures for a particular compound (e.g., to achieve maximum solubility or other desirable properties) was conventional and routine in the art at the time of the invention. Further, as Elstner teaches dissolving co Q10 in a mixture of γ-terpinene (an isomer of d-limonene) and vitamin E, the artisan of ordinary skill would have expected co Q10 to be soluble in a mixture of d-limonene and vitamin E.

Additionally, under the doctrine of In re: Kerkhoven, it would have been obvious to one of ordinary skill in the art to combine solvents in which co Q10 is known to be soluble, i.e., d-limonene, rice bran oil and vitamin E, to prepare a solution of co Q10 in this solvent mixture, because each solvent has been shown in the prior art to be particularly effective for delivering co Q10 to cells in humans. It is *prima facie* obvious to combine two or more compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose, as the idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). One of ordinary skill in the art would have reasonably expected to have been able to combine the solvent mixture of Soft Gel with the solvent of Garti et al. to produce a co Q10 solution with improved bioavailability, because both have been demonstrated in the prior art to work for this purpose. Thus, the combination of the teachings of Garti et al. and Soft Gel with respect to preparing solutions of co Q10 is an obvious combination. See claims 19, 37-39, 41, 47-49 and 51.

Regarding claims 47-49 and 51, which recite a neutraceutical composition packaged with instructions, because the composition of Soft Gel is a neutraceutical, it would have been obvious to the artisan of ordinary skill at the time of the invention to package it for sale as

neutraceutical, along with instructions for its use.

Regarding the concentration range recited in these claims (a 15-60% solution by weight of co Q10 in limonene), as discussed above, Garti et al. do not disclose the solubility limit of co Q10 in d-limonene. They disclose, however, that, in the concentrated form of their composition, the oil phase contains 2.45% co Q10 and 17.22% d-limonene, as percentages of the whole (see paragraph 40). But, the ranges recited in the claims do not appear to be associated with any particular result or effect. It would have been obvious to one of ordinary skill in the art at the time of the invention to dissolve as much co Q10 as possible in the limonene and in the solvent mixtures of limonene and one or more additional oils (such as rice bran oil, vitamin E, or rice bran oil and vitamin E) in order to make the most concentrated preparation possible, in order to deliver as much co Q10 as possible to the body. The solubility limit of co Q10 in any solvent or solvent mixture would have been readily determined by the artisan of ordinary skill, such a determination being routine in the art. The maximum solubility of a compound in a solvent or solvent mixture is an inherent property of that liquid.

Claims 40 and 50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Soft Gel Technologies, Inc. (EP 888774) in view of Garti et al. (US 2003/0232095 A1), Elstner (WO 02/09685 A1 or English language equivalent US 2004/0047922 A1), and Davidson et al. (US 2004/0001874). The teachings of Soft Gel, Garti et al. and Elstner are discussed above.

To reiterate, regarding claims 40 and 50, Davidson et al. disclose soft gel capsules containing fish oil into which co Q10 is blended. Fish oil reduces serum triglyceride levels and reduces the incidence of death from cardiovascular disease. Patients with cardiovascular disease often take statin drugs, which deplete the body's coQ 10, thereby causing muscle toxicity (myopathy) (see paragraphs 55 and 57). The soft gel capsules of Davidson et al.

replenish the co Q10 in the body and also treat hypertriglyceridemia. It would have been obvious to one of ordinary skill in the art at the time of the invention to add fish oil as a carrier oil to the contents of the soft gel of Soft Gel, in addition to adding the solvent of Garti et al., to add an extra neutraceutical ingredient, because Davidson et al. disclose that soft gels containing co Q10 and fish oil can both treat high triglyceride levels and provide co Q10 to humans. Moreover, the artisan of ordinary skill would have expected the co Q10 to be soluble in the fish oil, as co Q10 is a very lipophilic compound that is insoluble in water and hydrophilic solvents but soluble in oils, such as long-chain fatty acids, which are the components of fish oil (similarly to some of the solvents of Garti et al.). The artisan of ordinary skill also would have expected the fish oil to be miscible with the d-limonene and a lipophilic carrier, such as rice bran oil, based on the chemical structures and hydrophobicity of these molecules.

Regarding claim 50, which recites a neutraceutical composition packaged with instructions, because the composition of Soft Gel is a neutraceutical, it would have been obvious to the artisan of ordinary skill at the time of the invention to package it for sale as neutraceutical, along with instructions for its use.

Regarding the concentration range recited in these claims (a 15-60% solution by weight of co Q10 in limonene), as discussed above, Garti et al. do not disclose the solubility limit of co Q10 in d-limonene. They disclose, however, that, in the concentrated form of their composition, the oil phase contains 2.45% co Q10 and 17.22% d-limonene, as percentages of the whole (see paragraph 40). But, the ranges recited in the claims do not appear to be associated with any particular result or effect. It would have been obvious to one of ordinary skill in the art at the time of the invention to dissolve as much co Q10 as possible in the limonene and in the solvent mixtures of limonene and one or more additional oils (one to three oils from among rice bran oil, vitamin E and fish oil) in order to make the most concentrated preparation possible, in order to

deliver as much co Q10 as possible to the body. The solubility limit of co Q10 in any solvent or solvent mixture would have been readily determined by the artisan of ordinary skill, such a determination being routine in the art. The maximum solubility of a compound in a solvent or solvent mixture is an inherent property of that liquid.

As noted above, Applicant has not argued the dependent claims separately. Therefore, these claims are obvious for the reasons discussed above.

In view of the foregoing, a holding of obviousness is again required.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROSANNE KOSSON whose telephone number is (571)272-2923. The examiner can normally be reached on Mon., Tues., Fri., 8:30-6:00, Thurs., 8:30-2:00, Wed. off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rosanne Kosson/
Examiner, Art Unit 1652
2011-01-06